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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/471,669	12/24/1999	JOHN P. ANDERSON	00228-US-NEW	7795

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EXAMINER

WALICKA, MALGORZATA A

ART UNIT PAPER NUMBER

1652

DATE MAILED: 12/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/471,669

Applicant(s)

ANDERSON ET AL.

Examiner

Malgorzata A. Walicka

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1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 June 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.

4a) Of the above claim(s) 1-47 is/are withdrawn from consideration.

- 5) ☒ Claim(s) See Continuation Sheet is/are allowed.

- 6) ☒ Claim(s) See Continuation Sheet is/are rejected.

- 7) ☒ Claim(s) The following claim are objected:

58-59, 62, 68-69, 119, 121, 127, 129, 151, 153, 167, 169, 175, 177-183, 191-192, 194-195, 197-198, 200, 209-210, 212, 310-315, 340-357 and 282-296. is/are objected to.

- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.

- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some * c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-48,51-62,64-69,114-182,184-188,190-194,196-200,202-206,208-212,214-218,220-224 and 226-391.

Continuation of Disposition of Claims: Claims allowed are 114-116,122-124,146-148,162-164,170-172,184-189,202-206,214-218,220-224,226-277,316-333 and 373-390.

Continuation of Disposition of Claims: Claims rejected are 48-58,61,64-67,117,118,120,125,126,128,130-145,149,150,152,154-161,165,166,168,173,174,176,190,193,196,199,208,211,278-281,297-300 and 335-338.

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Petition for revival of an application for patent abandoned unintentionally under 37 CFR 1.137(b)

was filed in this application on June 26, 2006. The petition has been granted on August 14, 2006.

A request for continued examination under 37 CFR 1.114 filed June 26, 2006 and amendment under 37 CFR 1.116 filed June 5, 2006 are acknowledged. The request for continued examination includes the fee set forth in 37 CFR 1.17(e). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the Office action of December 16, 2005 has been withdrawn pursuant to 37 CFR 1.114.

In amendment filed June 5, 2006 claims 1-47 have been withdrawn. Claims 63, 183, 189, 195, 201, 207, 213, 219 and 225 have been cancelled; claims 49-50, and 70-113 have been previously canceled. Claims 48, 58, 64, 114, 122, 130, 138, 146, 154, 162, 170, 178, 184, 190, 196, 202, 208, 214, 220, 240, 259, 278, 297, 316, 335, 354, 373 have been amended, and claims 316-391 have also been amended due to renumbering of the claims after claim 312. Claims after claim 312 had previously wrong numbering due to typographical error of duplication numbers 311 and 312 in numbering of the claims. Claims 1-48, 51-62, 64-69, 114-182, 184-188, 190-194, 196-200, 202-206, 208-212, 214-218, 220-224 and 226-391 are pending. Claims 1-47 are withdrawn as directed to non-elected invention. This Office action uses current corrected numbering of the claims.

Detailed Action

1. Objections

Claim 48, 114, 122, 131, 139, 147, 155, 163 and 171 were objected to in the final rejection of Dec. 16, 2005 (final rejection). The objection is now withdrawn, because the claims have been amended.

Claim 130 is objected to as containing typographical error "SEQ ID NO: 43" in the second line. The correct sequence number is 66.

Claims 304 and 305 contain double period after the claim number. Please correct.

Claim 192 contains two comas after 191 in the first line.

Claim 206 contains two comas after 205 in the first line.

Claim 286 contains two comas after 281 in the first line.

Claim 306 contains two comas after 300 in the first line.

Examiner's suggestion

The examiner suggests cancellation of claims 1-47 directed to a nonelected invention.

21. Rejections

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2.1. 35 U.S.C. 112, second paragraph

1. Claim 48, 114, 122, 130, 138, 146, 154, 162 and 170, were finally rejected under 35 U.S.C. 112, second paragraph, as being still confusing. Dependent claims 51-57, 115-121, 123-129, 131-137, 139-145, 147-153, 155-161, 163-169, 171-177 were included in the rejection, because they did not correct the language of the claims from which they depend.

Rejection of claims 48, 51-57 and 114-177 is withdrawn, because the claims have been amended.

Furthermore, claims 58-69,

claims 178-183 and 240-258,

claims 184-189 and 259-277,

claims 190-195 and 278-296,

claims 196-201 and 297-315,

claims 202-207 and 316-334,

claims 208-213 and 335-353,

claims 214-219 and 354-372, and

claims 220-224 and 373-391 were rejected because the base claims 58, 178, 184, 190, 196, 202, 208, 214, 220 were confusing. Rejection of claims 58-62, 64-69, 178-182 and 240-258, 184-188 and 259-277, 190-194 and 278-296, 196-200 and 297-315, 202-206 and 316-334, 208-212 and 335-353, 214-218 and 354-372, 220-224 and 373-391 is withdrawn because the claims have been amended. Rejection of claims 63,

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183, 189, 195, 201, 207, 213, 219, 225 is moot because the claims have been cancelled.

2. Claims 53-57, claim 64-69, claim 117-121, claim 25-129, 133-137, 141-145, 149-153, 157-161, 165-169, 173-177, 240, 259, 278, 297, 316, 335, 354, 373 are rejected as confusing as to whether the heterologous transfected cell is in a transgenic animal or it is an isolated heterologous cell.

The examiner suggest the language " An isolated heterologous cell".

3. Claims 335 and 354 are unclear as to the language of part (i). For examination purposes it is assumed that he intended language is: (i) a nucleic acid molecule comprising a nucleotide sequence encoding etc.

2.2. 35 USC, first paragraph

Claim 63, 183, 189, 195, 201, 207, 213, 219 and 225 were rejected under 35 U.S.C. 112, for the reasons explained in the previous Office actions.

This rejection is now moot because claims 63, 183, 189, 195, 201, 207, 213, 219 and 225 have been cancelled.

2.3.35 U.S.C. 102

A. *DNA molecules encoding beta secretase having amino acid sequence shorter than SEQ ID NO: 2*

A1. Claims 48, 51-57, 130-137, 138-145 and 154-161 are rejected in the as anticipated by the US Patent 6, 420,534 issued to Gurney et al., with priority to the provisional application 60/101,594 ('594) filed Sept. 24, 1998. The claims recite

SEQ ID NO: 43 (amino acids 46-501),

SEQ ID NO: 66 (amino acids 22-501),

SEQ ID NO: 67 (amino acids 58-501),

SEQ ID NO: 69 (amino acids 63-501).

The scope of the claimed DNA molecules comprises SEQ ID NO: 1 of this application (SEQ ID NO: 5 of Gurney) because SEQ ID NO: 1 **comprises**

codons 46 –501 encoding beta secretase of SEQ ID NO: 43,

codons 22 –501 encoding beta secretase of SEQ ID NO: 66,

codons 58 –501 encoding beta secretase of SEQ ID NO: 67,

codons 63 –501 encoding beta secretase of SEQ ID NO: 69,

It is an inherent feature of SEQ ID NO: 1 (SEQ ID NO: 5 in Gurney) that expression thereof in an isolated heterologous cells **produces** a protein consisting of **amino acids 22-501, 46-501, 58-501 and 63-501 of SEQ ID NO: 2**, even if Gurney has not disclosed it. Gurney, in addition, teaches expression vectors, and isolated heterologous cells transfected with said vectors.

A2. On the other hand, **the polypeptides having truncated C-terminus, i.e.,**

SEQ ID NO: 58 (amino acids 46-452),

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SEQ ID NO: 59 (amino acids 1-452),

SEQ ID NO: 68 (amino acids 58-452),

SEQ ID NO: 70 (amino acids 63-452),

SEQ ID NO: 74 (amino acids 22-452),

are encoded, **among other DNA molecules**, by SEQ ID NO: 1 (SEQ ID NO in Gurney).

However, SEQ ID NOs: 58, 59, 68, 70, 74 **are not inherently expressed from SEQ ID NO: 1** of the instant application or SEQ ID NO: 5 of Gurney.

A3. Examiners explanations and suggested claims language

Applicants are the first to disclose that SEQ ID NO: 1 of the instant application (SEQ ID NO: 5 in Gurney) is expressed to result in beta-secretases of SEQ ID NOs: 43, 66, 67, and 69. Thus, of SEQ ID NOs: 43, 66, 67, and 69 are novel and nonobvious, and so are the **DNA molecules obtained by translation** of these sequences.

To overcome the rejection of claims 48, 51-57, 130-137, 138-145 and claims 154-161 the examiner suggest the following language for independent claims 48, 130, 138 and 154:

an isolated nucleic acid consisting of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 43 (66, 67, and 69) or a perfectly complementary sequence thereof.

B. Method of producing a recombinant beta secretase shorter than SEQ

ID NO: 2

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Claims 58, 190, 196 and 208 are rejected over Gurney et al as directed to a method of producing a recombinant beta-secretase enzyme by a cell transfected with a vector comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 43 (66, 67, 69) and applying affinity matrix for purification of the produced protein.

As explained above in part A, **it is an inherent feature** of SEQ ID NO: 1 (SEQ ID NO: 5 in Gurney) that expression thereof in an isolated heterologous cells **produces** a protein consisting of **amino acids 22-501 (SEQ ID NO: 66), 46-501 (SEQ ID NO: 43, 58-501 (SEQ ID NO: 67) and 63-501 (SEQ ID NO: 69) of SEQ ID NO: 2**, even if Gurney has not disclosed it. Gurney, in addition, teaches expression vectors, and isolated heterologous cells transfected with said vectors, as well as affinity chromatography for purification of expressed protein; see page 9 line 18 of the 60/105,594. Gurney et al teach all the elements of the rejected claims.

The examiner suggest limiting the claims to "A method of producing a recombinant beta-secretase of SEQ ID NO: 43 comprising culturing a cell transfected with a vector comprising the isolated nucleic acid consisting of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 43 (66, 67, and 69) etc."

2.4. 35 USC 103

Heterologous cell comprising beta secretase DNA and beta secretase substrate DNA

Claims 64-67(SEQ ID NO: 43); 278-281 (SEQ ID NO: 66); 297-300(SEQ ID NO: 67); 335-338 (SEQ ID NO: 69) are rejected under 35 U.S.C. 103(a) as being unpatentable over Patent 6,420,534 issued to Gurney et al., with priority to the provisional application 60/101,594 ('594) filed Sept. 24, 1998 and a routine practice in the art of expressing enzymes in heterologous cells.

The claims are directed to a heterologous cell, comprising

- (i) a nucleic acid molecule comprising a nucleotide sequence encoding the beta-secretase consisting of SEQ ID NO: 43 (66, 67 and 69) or a perfectly complementary sequence thereof,
- (ii) a nucleic acid encoding a beta-secretase substrate molecule; and
- (iii) operatively linked to (i) and (ii) a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

As explained in the above rejection under 35 USC 102, Gurney et al disclose DNA molecule comprising the polynucleotide (SEQ ID NO:5, Hu-AsP) sequence encoding beta secretase consisting of SEQ ID NO: 43, 66, 67, and 69. Furthermore Gurney et al teaches human embryonic kidney cell line HEK293 is preferably used for expression of Hu-AsP2; see page 11, line 20. In addition Gurney et al. teaches cotransformation of HEK293 with plasmids containing HU-AsP and its a substrate (page 26 line 10 of 60/101,594). The substrate is human APP or its Swedish mutation. The cotransformed non-heterologous HEK293 is used in a cellular assays for inhibitors of beta-secretase; see pages 23-28 of the Gurney's provisional application. Gurney et al also teach many heterologous cell lines and suitable vectors for expression of AsP2(b).

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It would have been obvious for one having skills in the art to modify teachings of Gurney et al. by replacing human (homologous) cells with a nonhuman heterologous cells. The motivation of one having skills in the art would be to have a recombinant heterologous cell for an assay for beta secretase inhibitors because one skilled in the art realizes that non-human cells are easier to grow in vitro and are usually more reproducible in the in vitro assays.

Claims 68-69, 282-296, 301-315, 339-353 are objected to as depending on claims rejected under this paragraph.

Method of producing a and purifying recombinant beta secretase shorter than SEQ ID NO: 2

Claims 61, 193, 199 and 211 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patent 6,420,534 issued to Gurney et al., with priority to the provisional application 60/101,594 ('594) filed Sept. 24, 1998 and a routine practice of protein purification using affinity matrix, wherein affinity matrix contains antibodies having abilities to bind said protein.

As explained in the above rejection under 35 USC 102, Gurney et al disclose DNA molecule comprising the polynucleotide (SEQ ID NO:5, Hu-AsP) sequence encoding beta secretase consisting of SEQ ID NO: 43, 66, 67, and 69. Gurney et al. also teach production of antibodies directed to Hu-Asp, including HuAsp2(b) - page 12 of ('594), the first paragraph.

I would have been obvious for one having skills in the art at the time of invention to use SEQ ID NO: 5 of Gurney et al. and to produce recombinantly beta secretases consisting of SEQ ID NO: 43, 66, 67, and 69 and then purify the beta secretases using affinity matrix containing antibodies having abilities to bind said beta secretase disclosed by Gurney, i.e. beta secretase of SEQ ID NO of the instant application.

2.5. Double patenting rejection

Provisional obviousness type double patenting rejection withdrawal

Rejection of claims 48, 51-69, and 114-390 were provisionally rejected over claims of 09/724,569 is withdrawn, because Applicants filed on April 21, 2006 a proper terminal disclaimer.

Provisional statutory double patenting rejection

Rejection of claim 114, 48, 131, and 171 made in previous Office Action because they are claiming the same invention as claims 57-60 of the US application No. 09/724,569 is moot, because claims 57-60 of the US application No. 09/724,569 have been cancelled.

3. Conclusion

All claims related to the DNA encoding human beta secretase truncated from C-terminus identified by SEQ ID NO: 58 (amino acids 46-452), SEQ ID NO: 59 (amino acids 1-452), SEQ ID NO: 68 (amino acids 58-452), SEQ ID NO: 70 (amino acids 63-452) and SEQ ID NO: 74 are allowable for reasons indicated in previous Office Actions and above, if not for objections and rejections under 35 USC 112, second paragraph.

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The following claims are allowed:

114-116, 122-124, 146-148, 162-164, 170-172, 184-189, 202-206, 214-218, 316-333, 220-224, 226-277, 316-333 and 373-390.

The following claims are rejected:

48-58, 61, 64-67, 117-118, 120, 125-126, 128, 130-145, 149-150, 152, 154-161, 165-166, 168, 173-174, 176, 190, 193, 196, 199, 208, 211, 278-281, 297-300 and 335-338.

The following claim are objected:

58-59, 62, 68-69, 119, 121, 127, 129, 151, 153, 167, 169, 175, 177-183, 191-192, 194-195, 197-198, 200, 209-210, 212, 310-315, 340-357 and 282-296.

As allowable subject matter has been indicated, applicant's reply must either comply with all formal requirements or specifically traverse each requirement not complied with. See 37 CFR 1.111(b) and MPEP § 707.07(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.


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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Malgorzata A. Walicka, Ph.D.

Art Unit 1652

Patent Examiner



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